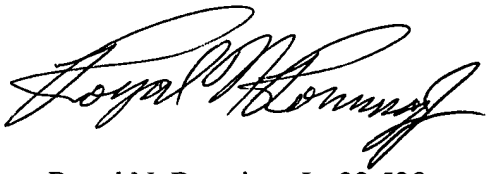
Applicants respectfully assert that all amendments are fairly based on the specification, and respectfully request their entry.

Applicants believe that the claims, as amended, are in allowable form, and earnestly solicit the allowance of claims 1-29.

Respectfully submitted,



Royal N. Ronning, Jr. 32,529
Attorney for Applicants

Amersham Pharmacia Biotech, Inc.
800 Centennial Avenue
P. O. Box 1327
Piscataway, New Jersey 08855-1327

Tel: (732) 457-8423
Fax: (732) 457-8463

Claims (marked-up version showing amendment(s))

[C L A I M S]

What is claimed is:

4. (once amended) The method of [any of claims 1 to 3]claim 1, wherein the assay reagent is a compound which contains an artificially high concentration of an NMR active nucleus.

6. (once amended) The method of [any of claims 1 to 5]claim 1, wherein the assay reagent is an organic compound comprising one or more NMR active nuclei associated with a bond which is broken during the course of the assay.

8. (once amended) The method of [any claim 1-7]claim 1, wherein the assay reagent is analysed repeatedly in step c) at known time intervals so as to generate information about a change with time of the assay reagent.

9. (once amended) The method of [any one claim 1 to 8]claim 1, wherein the [asseay]assay reagent is a Nucleotide, or nucleotide analogue, polynucleotide, amino acid analogue, polypeptide or protein.

10. (once amended) The method of [any one of claims 1 to 9]claim 1, wherein the

assay is a nucleic acid hybridisation assay.

11. (once amended) The method of [any one of claims 1 to 10]claim 1, wherein the assay is a binding assay.

12. (once amended) The method of [claims 1 to 11]claim 1, wherein the assay reagent is a compound specifically labelled with at least one NMR active nucleus and the assay reagent is administered to a micro-organism, macro-organism or cultured cells, cellular metabolites or an excretion product of the assay reagent are hyperpolarised and analysed by nuclear magnetic resonance spectroscopy, nuclear magnetic resonance imaging or both.

13. (once amended) The method of [claims 1 to 12]claim 1, wherein the assay is a binding study performed using micro-organisms or cultured cells

14. (once amended) The method of [claims 1 to 13]claim 1 wherein the hyperpolarisation transfer is repeated to enhance the signal-to-noise ratio.

15. (once amended) The method of [claim 1 to 14]claim 1 wherein the shortening effect as expressed by the improvement of signal-to-noise per unit time is a factor of 10 or more compared to known assay techniques without hyperpolarisation.

16. (once amended) The method of [claims 1 to 15]claim 1 where the hyperpolarisation of the NMR active nucleus of the assay reagent is carried out by polarisation transfer from a hyperpolarised noble gas, or a mixture of hyperpolarised noble gases.

19. (once amended) The method of [claims 16 to 18]claim 16 wherein the hyperpolarisation is transferred by a hyperpolarised noble gas in solution and wherein the viscosity of the solution is at least 1000 mPs.

20. (once amended) The method of [claims 1 to 15]claim 1 where the hyperpolarisation of the NMR active nucleus of the assay reagent is carried out by polarisation transfer at a temperature of 4.2 K or less in the presence of a magnetic field of at least 1 T.

21. (once amended) The method of [claims 1 to 15]claim 1 where the hyperpolarisation of the NMR active nucleus of the assay reagent is carried out by polarisation transfer using dynamic nuclear polarisation.

22. (once amended) The method of [claims 1 to 15]claim 1 where the hyperpolarisation of the NMR active nucleus of the assay reagent is carried out by para hydrogen induced polarisation.

23. (once amended) The method of [claims 1 to 15]claim 1 where the hyperpolarisation of the NMR active nucleus of the assay reagent is carried out with the spin refrigeration technique.

24. (once amended) The method of [claims 1 to 23]claim 1, wherein more than one assay is multiplexed and monitored by NMR spectroscopy and/or NMR imaging.

25. (once amended) The method of [claims 1 to 24]claim 1 wherein the assay is performed in a multiwell or multispot assay array.

26. (once amended) The method of [claims 1 to 25]claim 1 wherein step c) is performed by examining the assay reagent using both NMR spectroscopy to obtain more than one spectrum, and magnetic resonance imaging to obtain one or more discrete spectral location, and repeating the examination at least once so as to obtain quantitative information about kinetic or time-dependant alteration in chemistry, environment or structure of the assay reagent.

27. (once amended) The method of [claim 1 to 26]claim 1, wherein step c) is performed in an aerosol or flow-through device applied to aerosol droplets where the well, surface or container is used to contain the assay reagent.

28. (once amended) An *in vitro* assay kit for carrying out the assay method as defined

in claim 1 [to 27]which comprises: one or more assay reagents each containing at least one NMR active nucleus contained in a well or vial or other suitable container for carrying out the hyperpolarisation of step (b) of claim 1.

29. (once amended) The *in vitro* kit of claim 28 where the NMR analysis of step (c) [of claim 1] is carried out in the same well, vial or container as the hyperpolarisation transfer is carried out.